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EXAMINER	
BERTAGNA, ANGELA MARIE	
ART UNIT	PAPER NUMBER
1637	

NOTIFICATION DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/553,376	INOSE ET AL.	
	Examiner	Art Unit	
	Angela M. Bertagna	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 September 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5,9 and 10* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,9 and 10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on September 1, 2009 has been entered.

Claims 1-5, 9, and 10 are currently pending and are the subject of this Office Action.

Claim Rejections - 35 USC § 112, 2nd paragraph

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 2 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 2 contains the trademark/trade name Triton X-100. Where a trademark or trade name is used in a claim as a limitation to identify or describe a particular material or product, the claim does not comply with the requirements of 35 U.S.C. 112, second paragraph. See *Ex parte Simpson*, 218 USPQ 1020 (Bd. App. 1982). The claim scope is uncertain since the trademark or trade name cannot be used properly to identify any particular material or product. A trademark or trade name is used to identify a source of goods, and not the goods themselves. Thus, a trademark or trade name does not identify or describe the goods associated with the trademark or

trade name. In the present case, the trademark/trade name is used to identify/describe a non-ionic surfactant and, accordingly, the identification/description is indefinite.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

4. Claims 1, 3, 4, 9, and 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lurquin et al. (Analytical Biochemistry (1975) 65: 1-10; cited previously) in view of Vosbeck et al. (The Journal of Biological Chemistry (1973) 248(17): 6029-6034; cited previously) and further in view of Werner et al. (Plant Molecular Biology Reporter (1998) 16: 295-299; cited previously).

These claims are drawn to a method for isolating nucleic acids from a sample comprising eukaryotic cells and amplifying the isolated nucleic acids by PCR. The method comprises dissolving the sample in a buffer comprising a surfactant and a salt of a monovalent cation, heating the resulting solution at 80-100°C, performing gel filtration to obtain a solution containing nucleic acids, and amplifying a target DNA in the solution by PCR.

Lurquin teaches a method for isolating nucleic acids from eukaryotic cells (see abstract and page 3).

Regarding claims 1, 3, 9, and 10, the method of Lurquin comprises the following steps: (see page 3, 1st paragraph of the "Results and Discussion" section):

(a) dissolving a sample in a buffer comprising at least one surfactant and at least one salt of a monovalent cation (*i.e.* the saline-EDTA buffer comprising sodium sarcosylate),

(b) heating the obtained solution at 37°C,

(c) adding additional NaCl to a final concentration of 2M,

(d) removing PCR inhibitory substances by subjecting the heated solution to gel filtration, and

(e) collecting a solution fraction containing nucleic acids.

Regarding claim 4, the *Chlamydomonas reinhardi* cells used in the method of Lurquin are eukaryotic cells.

Lurquin does not teach heating the solution at a temperature within the claimed ranges of 80-100°C, 90-100°C, and 95-100°C. Also, Lurquin teaches adding NaCl to a final concentration of 2M after the heating step rather than before the heating step as required by claim 1.

Vosbeck studied the properties of the mixture of enzymes known as pronase (see abstract). Regarding claims 1, 9, and 10, Vosbeck teaches that pronase activity is eliminated at high temperatures, specifically temperatures above 80°C (see Figure 8).

Neither Lurquin nor Vosbeck teaches PCR amplification of isolated nucleic acids.

Werner teaches a PCR-based method for determining the mating type of *Chlamydomonas reinhardi* (see abstract and pages 296-297). The method of Werner comprises isolating DNA from *Chlamydomonas reinhardi* and amplifying the isolated DNA by PCR (pages 296-297).

It would have been *prima facie* obvious for one of ordinary skill in the art at the time of invention to add NaCl to a final concentration of 2M to the saline/EDTA/surfactant buffer used in the method of Lurquin before conducting the heating step. As noted in MPEP 2144.04 IV C, the selection of any order of mixing ingredients is *prima facie* obvious in the absence of unexpected results. In this case, there is no particular reason for adding the sodium chloride before or after the heating step, and therefore, in the absence of unexpected results, the claimed order of addition is *prima facie* obvious. Also, it would have been obvious for one of ordinary skill in the art at the time of invention to include a high temperature heating step in the method of Lurquin. An ordinary artisan would have been motivated to do so in order to ensure pronase inactivation. An ordinary artisan would have been particularly motivated to use a temperature within the claimed ranges, since Vosbeck taught that pronase was inactivated at 90°C (Figure 8). Finally, it would have been *prima facie* obvious for one of ordinary skill in the art at the time of invention to amplify the DNA isolated by the method resulting from the combined teachings of Lurquin and Vosbeck by PCR. An ordinary artisan would have been motivated to do so with a reasonable expectation of success, since Werner taught that this was a rapid, simple, and reliable

method for determining the mating type of a *Chlamydomonas reinhardi* strain (see abstract and pages 296-297). Thus, the methods of claims 1, 3, 4, 9, and 10 are *prima facie* obvious over Lurquin in view of Vosbeck and further in view of Werner in the absence of unexpected results.

5. Claim 2 is rejected under 35 U.S.C. 103(a) as being unpatentable over Lurquin et al. (Analytical Biochemistry (1975) 65: 1-10; cited previously) in view of Vosbeck et al. (The Journal of Biological Chemistry (1973) 248(17): 6029-6034; cited previously) and further in view of Werner et al. (Plant Molecular Biology Reporter (1998) 16: 295-299; cited previously) and further in view of Wilson et al. (US 7,045,679 B1; cited previously).

Claim 2 is drawn to the method of claim 1, wherein the surfactant is Triton X-100.

The combined teachings of Lurquin, Vosbeck, and Werner result in the methods of claims 1, 3, 4, 9, and 10, as discussed above.

Lurquin teaches that the surfactant is sodium sarcosylate rather than Triton X-100 (see page 3, 1st paragraph of the "Results and Discussion" section).

Wilson teaches a method for isolating nucleic acids from plant cells (see Example 1 at column 7).

Regarding claim 2, Wilson teaches the use of Triton X-100 in the lysis buffer (column 7, lines 16-19).

It would have been *prima facie* obvious for one of ordinary skill in the art at the time of invention to substitute Triton X-100 for sodium sarcosylate when practicing the method resulting from the combined teachings of Lurquin, Vosbeck, and Werner. Since Wilson taught that Triton X-100 could be used as the surfactant in a lysis buffer used in a method of isolating nucleic acids

from plant cells, an ordinary artisan would have recognized that Triton X-100 and sodium sarcosylate were art-recognized equivalents useful for the same purpose, and therefore, would have been motivated to substitute one for the other with a reasonable expectation of success. As noted in MPEP 2144.06 II, the substitution of art-recognized equivalents known to be useful for the same purpose is *prima facie* obvious in the absence of secondary considerations. Thus, the method of claim 2 is *prima facie* obvious in view of the combined teachings of the cited references.

6. Claims 1-5, 9, and 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Burdick et al. (EP 0 393 744 A1; cited previously) in view of Akane et al. (Biotechniques (1994) 16(2): 235, 237, 238; cited previously).

These claims are drawn to a method for isolating nucleic acids from a sample comprising eukaryotic cells, specifically a blood sample. The method comprises dissolving the sample in a buffer comprising a surfactant and a salt of a monovalent cation, heating the resulting solution at 80-100°C, and performing gel filtration to obtain a solution containing nucleic acids.

Burdick teaches methods for isolating nucleic acids from whole blood or peripheral blood mononuclear cells (see abstract and Example 2 at column 14, lines 26-44).

Regarding claims 1, 9, and 10, the method of Burdick comprises:

(a) dissolving a sample in a buffer comprising at least one surfactant and at least one salt of a monovalent cation (column 14, lines 32-39)

(b) heating the obtained solution at 80-100°C (column 14, lines 39-41 teaches heating at 118°C; column 6, lines 33-37 teach heating at 80-120°C or 95-120°C; column 6, lines 16-19 teach heating at 100°C)

(c) filtering the heated solution (column 6, lines 52-57 and column 14, lines 41-42)

(d) collecting a solution fraction containing nucleic acids (column 6, lines 52-57 and column 14, lines 41-42)

(e) amplifying an object DNA from the fraction containing nucleic acids by PCR (column 14, line 40 – column 15, line 3).

Regarding claim 2, Burdick teaches that the surfactant is Triton X-100 (column 14, lines 37-38).

Regarding claim 3, Burdick teaches that the salt is NaCl (column 14, lines 38-39).

Regarding claims 4 and 5, Burdick teaches that the sample is a blood sample that comprises eukaryotic cells (column 14, lines 25-35).

Burdick teaches filtering the heated solution through a membrane filter (column 6, lines 52-57 and column 14, lines 41-42), but does not teach conducting a gel filtration step as required by claim 1. Also, Burdick teaches using NaCl at a concentration of 0.5 to 1.5 weight percent (86 mM – 257 mM), rather than a value within the claimed concentration range of 0.5 - 2 M.

Akane teaches methods of preparing DNA samples for PCR comprising a gel filtration step (page 235). Regarding claim 1, Akane teaches that degraded DNA and a hemoglobin derivative (hematin) isolated from forensic samples interfere with PCR amplification (page 235, column 2). Akane further teaches that although contaminating hematin may be removed by treatment with bovine serum albumin, ultrafiltration, chelating resin treatment, gel filtration or

anion-exchange chromatography, degraded DNA may only be removed using gel filtration (page 235, column 2).

It would have been *prima facie* obvious for one of ordinary skill in the art at the time of invention to incorporate a gel filtration step into the nucleic acid purification method taught by Burdick. Since the method of Burdick comprised a PCR amplification step following nucleic acid isolation (column 14, lines 41-44), an ordinary artisan would have been motivated to incorporate a gel filtration step, as suggested by Akane, in order to remove any contaminating degraded DNA fragments that would interfere with the PCR. An ordinary artisan would have had a reasonable expectation of success in incorporating a gel filtration step into the method of Burdick since both methods were directed to purification of DNA from forensic samples for PCR analysis.

It also would have been *prima facie* obvious for one of ordinary skill in the art at the time of invention to optimize the NaCl concentration when practicing the nucleic acid isolation method resulting from the combined teachings of Burdick and Akane. An ordinary artisan would have been motivated to optimize this results-effective variable in order to improve salt-induced precipitation of contaminating proteins present in the sample prior to the filtration step. As noted in MPEP 2144.05, "Generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. '[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation.' *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235

(CCPA 1955) (MPEP 2144.05)." Routine optimization is not inventive and there is no evidence to suggest that the selection of the claimed salt concentrations was other than routine or that the results should be considered unexpected compared to the closest prior art. Thus, the methods of claims 1-5, 9, and 10 are *prima facie* obvious over Burdick in view of Akane.

Response to Amendment

7. The declaration under 37 CFR 1.132 filed on September 1, 2009 is insufficient to overcome the following rejections as set forth in the last Office Action: (i) the rejection of claims 1, 3, 4, 9, and 10 under 35 U.S.C. 103(a) as being unpatentable over Lurquin in view of Vosbeck and further in view of Werner, (ii) the rejection of claim 2 under 35 U.S.C. 103(a) as being unpatentable over Lurquin in view of Vosbeck and further in view of Werner and further in view of Wilson, and (iii) the rejection of claims 1-5, 9, and 10 under 35 U.S.C. 103(a) as being unpatentable over Burdick in view of Akane. The declaration is insufficient to overcome these rejections, because: (i) The evidence presented is not commensurate in scope with the claimed invention, and (ii) The evidence does not establish that the results are statistically significant.

The declaration describes experiments conducted by one of the inventors (Satoshi Hashiguchi) in which DNA was isolated from a blood sample under different salt conditions and amplified by PCR (see points 7-11). Specifically, a blood sample was heated at 98°C for 5 minutes in a buffer comprising 0.1 M, 0.5 M, or 2 M NaCl, subjected to gel filtration using a commercially available spin column, and amplified by PCR (see points 7-9). The results submitted in the declaration suggest that the inclusion of 0.5 M or 2M NaCl in the buffer resulted

in the isolation of a higher yield and/or better quality DNA compared to that obtained using the 0.1 M NaCl solution (see points 10-11).

The evidence presented in the declaration not commensurate in scope with the claimed invention, because the evidence presented relates to only a very specific embodiment of the claimed methods, which are much broader in scope, and there is no evidence that the results described in the declaration would necessarily extend over the full scope of the claimed methods. As noted in MPEP 716.02(d), citing *In re Clemens*, 622 F.2d 1029, 1036, 206 USPQ 289, 296 (CCPA 1980), "Whether the unexpected results are the result of unexpectedly improved results or a property not taught by the prior art, the 'objective evidence of nonobviousness must be commensurate in scope with the claims which the evidence is offered to support.'"

In this case, with the exception of claim 5, which is limited to a blood sample, the claimed methods encompass the extraction, purification, and amplification of DNA from any sample (*e.g.* any bodily fluid obtained from any organism, any cell type, *etc*), whereas the results described in the declaration only relate to blood samples. Also, the experiments described in the declaration were conducted using only an incubation for a single length of time (5 minutes) at a single temperature at the upper end of the claimed ranges (98°C), whereas the claimed methods encompass any incubation time at temperatures between 80-100°C (see claims 1-5), 90-100°C (claim 9), and 95-100°C (claim 10). Furthermore, the experiments described in the declaration were conducted using a specific surfactant and monovalent salt (Triton X-100 and NaCl), whereas the claimed methods with the exception of claims 2 and 3, respectively, are not limited to a particular surfactant or monovalent salt. It is not clear from the evidence presented or the art that the observed results would necessarily extend over the full scope of the claimed methods,

since obtaining a sufficient quantity of PCR-amplifiable DNA from a sample typically involves different considerations specific to the sample type (*e.g.* susceptibility to thermal lysis, removal of inhibitors and contaminants, *etc*). Accordingly, the evidence presented in the declaration is not commensurate in scope with the claimed invention.

Also, it is not clear from the evidence presented in the declaration that the observed results are statistically significant. There is no discussion in the declaration regarding the statistical significance of the observed results or what results would have been reasonably expected for the different conditions tested. As noted in MPEP 716.02(a), citing *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986), "Any differences between the claimed invention and the prior art may be expected to result in some differences in properties. The issue is whether the properties differ to such an extent that the difference is really unexpected." Also, as noted in MPEP 716.02(b), citing *Ex parte Gelles*, 22 USPQ2d 1318, 1319 (Bd. Pat. App. & Inter. 1992),"The evidence relied upon should establish 'that the differences in results are in fact unexpected and unobvious and of both statistical and practical significance." Furthermore, as noted in MPEP 716.02(b), citing *Ex parte Ishizaka*, 24 USPQ2d 1621, 1624 (Bd. Pat. App. & Inter. 1992, "[A]ppellants have the burden of explaining the data in any declaration they proffer as evidence of non-obviousness."

In view of the foregoing, when all of the evidence is considered, the totality of the rebuttal evidence of nonobviousness fails to outweigh the evidence of obviousness.

Response to Arguments

8. Applicant's arguments filed on September 1, 2009 have been fully considered, but they were not persuasive.

Regarding the rejection of claims 1, 3, 4, 9, and 10 under 35 U.S.C. 103(a) as being unpatentable in view of the combined teachings of Lurquin, Vosbeck, and Werner, Applicant first argues that there is no reason to combine the teachings of Werner with those of Lurquin and Vosbeck (see page 2).

In response to this argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir.1992). In this case, as discussed previously and above, it would have been *prima facie* obvious for one of ordinary skill in the art at the time of invention to amplify the DNA isolated by the method resulting from the combined teachings of Lurquin and Vosbeck by PCR, since Werner taught that this was a rapid, simple, and reliable method for determining the mating type of a *Chlamydomonas reinhardi* strain (see abstract and pages 296-297).

Applicant also argues that Lurquin teaches increasing the salt concentration to 2 M salt after the heating step, whereas the claimed methods require that the heating step is conducted in the presence of high salt to effect the dissociation of histone proteins from DNA prior to their aggregation during the heating step (see pages 2-3).

This argument was not persuasive, because as discussed above, the teachings of Vosbeck would have suggested to the ordinary artisan that including a high-temperature pronase inactivation step in the method of Lurquin would provide the benefit of eliminating undesirable residual pronase activity. It would have been *prima facie* obvious for the ordinary artisan to conduct the high temperature pronase inactivation step suggested by Vosbeck at any point in the method disclosed by Lurquin following the 1 hour incubation with pronase at 37°C (*e.g.*, after the addition of the high salt solution and before the gel filtration step, after the 37°C incubation and before the addition of the high salt solution, or simultaneously with the addition of the high salt solution). As noted in MPEP 2144.04 IV C, the selection of any order of conducting process steps is *prima facie* obvious in the absence of unexpected results. In this case, there is no particular reason for selecting any of the above orders for conducting the process steps suggested by the combined teachings of the cited reference, and therefore, any of the above orders is *prima facie* obvious in the absence of secondary considerations with respect to the order of conducting the method steps. Also, as noted previously, the pronase digestion step taught by Lurquin would appear to inherently result in the degradation of DNA-associated histones, and therefore, the method resulting from the combined teachings of Lurquin, Vosbeck, and Werner would not appear to produce the aggregates described by Applicant as rendering the method unsuitable for subsequent PCR amplification.

Furthermore, in response to applicant's argument that the claimed methods do not recite the use of pronase and that Lurquin does not teach pronase inactivation (see page 3), the fact that applicant has recognized another advantage which would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would

otherwise be obvious. See *Ex parte Obiaya*, 227 USPQ 58, 60 (Bd. Pat. App. & Inter. 1985). In this case, as discussed above, the claimed methods do not exclude methods, such as those resulting from the combined teachings of Lurquin, Vosbeck, and Werner, in which a sample is incubated in a high salt buffer and simultaneously or subsequently subjected to a high-temperature pronase inactivation step prior to gel filtration and PCR amplification.

Finally, Applicant argues that the declaration submitted under 37 CFR 1.132 on September 1, 2009 is sufficient to overcome the rejection (see pages 3-4). This argument was not persuasive, because as discussed above, the declaration was insufficient to overcome the rejection of claims 1, 3, 4, 9, and 10 made under 35 U.S.C. 103(a) in view of the combined teachings of Lurquin, Vosbeck, and Werner.

Since Applicant's arguments were not persuasive, the rejection of claims 1, 3, 4, 9, and 10 made under 35 U.S.C. 103(a) as being unpatentable over Lurquin in view of Vosbeck and further in view of Werner has been maintained.

Regarding the rejection of claim 2 under 35 U.S.C. 103(a) as being unpatentable in view of the combined teachings of Lurquin, Vosbeck, Werner, and Wilson, Applicant argues that the rejection should be withdrawn, since the primary combination of references (Lurquin, Vosbeck, and Werner) does not teach or suggest all of the limitations of independent claim 1 from which claim 2 depends (see page 4). This argument was not persuasive, because as discussed above, the combined teachings of Lurquin, Vosbeck, and Werner render obvious the methods of claims 1, 3, 4, 9, and 10. Since Applicant's arguments were not persuasive, the rejection has been maintained.

Regarding the rejection of claims 1-5, 9, and 10 under 35 U.S.C. 103(a) as being unpatentable in view of the combined teachings of Burdick and Akane, Applicant first argues that the declaration submitted under 37 CFR 1.132 on September 1, 2009 is sufficient to overcome the rejection (see pages 4-5). This argument was not persuasive, because as discussed above, the declaration was insufficient to overcome the rejection of claims 1-5, 9, and 10 made under 35 U.S.C. 103(a) in view of the combined teachings of Burdick and Akane.

Applicant also argues that the ordinary artisan would have no motivation to increase the salt concentration to values known in the art to inhibit polymerase activity and then dilute the salt prior to conducting PCR amplification, because doing so may result in salt-mediated polymerase inhibition and also compromise the sensitivity of the PCR amplification step by reducing the amount of DNA available for PCR amplification (see pages 5-6). This argument was not persuasive, because as discussed previously, only a reasonable expectation of success in required to establish a *prima facie* case of obviousness under 35 U.S.C. 103(a) (MPEP 2143.02 I). In this case, as discussed previously, since Burdick expressly taught diluting the isolated nucleic acids prior to amplification, and since dilution factors, such as 50-fold or 25-fold, were routinely used in PCR amplification, an ordinary artisan would have had a reasonable expectation of success in practicing the method suggested by the combined teachings of Burdick and Akane and determining a suitable dilution factor via routine experimentation. Also, since salt concentrations that may lead to decreased polymerase activity were also known in the art as evidenced, for example, by the Chien reference cited previously by Applicant, an ordinary artisan would have had a reasonable expectation of success in balancing the optimization of the results-effective variables (*i.e.* the dilution factor and salt concentration) when conducting the

routine experimentation suggested by the combined teachings of Burdick and Akane. Since Applicant's arguments were not persuasive, the rejection has been maintained.

Conclusion

9. No claims are currently allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ANGELA BERTAGNA whose telephone number is (571)272-8291. The examiner can normally be reached on M-F, 9-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Angela M. Bertagna/
Examiner, Art Unit 1637

/Kenneth R Horlick/
Primary Examiner, Art Unit 1637